

### **Human Neutralizing Monoclonal Antibodies to Respiratory Syncytial Virus and Human Neutralizing Antibodies to Respiratory Syncytial Virus**

Inventors: Robert Chanock, Dennis Burton, Carlos Barbas III, Brian Murphy, and James Crowe Jr.

Serial Number 08/162,102 filed 10 Dec 93 (with priority to 16 Sep 92) which issued as U.S. Patent Number 5,762,905 on 09 Jun 98 and Serial Number 08/920,100 filed 26 Aug 97 (divisional of 08/162,102)

This invention is a human monoclonal antibody fragment (Fab) discovered utilizing phage display technology. It is described in Crowe et al., *P.N.A.S.* 91:1386-1390 (1994) and Barbas et al., *P.N.A.S.* 89:10164-10168 (1992). This MAb binds an epitope on the RSV F glycoprotein at amino acid 266 with an affinity of approximately  $10^9 \text{ M}^{-1}$ . This MAb neutralized each of 10 subgroup A and 9 subgroup B RSV strains with high efficiency. It was effective in reducing the amount of RSV in lungs of RSV-infected cotton rats 24 hours after treatment, and successive treatments caused an even greater reduction in the amount of RSV detected. The invention has been foreign filed as PCT/US93/08786.

### **Murine Monoclonal Antibodies Effective To Treat Respiratory Syncytial Virus**

Inventors: Robert Chanock, Brian Murphy, Judy Beeler, and Kathleen van Wyke Coelingh

Available for licensing through a Biological Materials License Agreement are the murine MAbs described in Beeler, J. A. et al. "Neutralization Epitopes of the F Glycoprotein of Respiratory Syncytial Virus: Effect of Mutation Upon Fusion function," *J. Virology* 63:2941-2950 (1989). The MAbs that are available for licensing are the following: 1129, 1153, 1142, 1200, 1214, 1237, 1121, 1112, 1269, and 1243. One of these MAbs, 1129, is the basis for a humanized murine MAb (see U.S. Patent Number 5,824,307 to humanized 1129 owned by MedImmune, Inc.), recently approved for marketing in the United States. MAbs in the panel reported by Beeler, et al. have been shown to be effective therapeutically when administered into the lungs of cotton rats by small-particle aerosol. Among these MAbs several exhibited a high affinity (approximately  $10^9 \text{ M}^{-1}$ ) for the RSV F glycoprotein and are directed at epitopes encompassing amino acid 262, 272, 275, 276 or 389. These epitopes are separate, nonoverlapping and distinct from the

epitope recognized by the human Fab of patent 5,762,905 (see above for description).

### **Immunotherapeutic Method of Preventing or Treating Viral Respiratory Tract Disease**

Inventors: Robert Chanock, Gregory Prince, James Young, Brian Murphy, Val Hemming, Judy Beeler, Kathleen Coelingh Serial Number 08/479,797 filed 97 Jun 95 (CIP of combined applications 07/555,091 and 07/937,909)

Rather than the use of a single monoclonal antibody to treat lower respiratory infections, this invention contemplates the use of a mixture of neutralizing, prophylactic and therapeutic monoclonal antibodies each directed to a specific epitope on the surface of a major viral protein (for example, the F glycoprotein of RSV) to treat infections. Utilizing a mixture of antibodies significantly lessens the possibility of escape mutants. This invention discloses an improved method of treating or preventing lower respiratory tract viral diseases through the administration of multiple neutralizing and therapeutic antibodies in a small particle aerosol. Prior to this invention, there has not been a convenient method of administration. Previously, small children and infants have only been able to use this therapy when incubated and attached to a ventilator. An aerosol nebulizer is utilized in this invention. Furthermore, a prophylactic, neutralizing, and therapeutic combination of various antiviral agents is also described.

Dated: December 28, 1998.

#### **Jack Spiegel,**

*Director, Division of Technology Development and Transfer, Office of Technology Transfer.* [FR Doc. 99-240 Filed 1-5-99; 8:45 am]

BILLING CODE 4140-01-M

## **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

### **National Institutes of Health**

#### **National Institute of Neurological Disorders and Stroke; Notice of Closed Meetings**

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and

the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

*Name of Committee:* National Institute of Neurological Disorders and Stroke Initial Review Group Neurological Sciences and Disorders A.

*Date:* February 18-19, 1999.

*Time:* 8:30 AM to 5 PM.

*Agenda:* To review and evaluate grant applications.

*Place:* Washington Marriott Wardman Park Hotel, 2660 Woodley Road, NW, Washington, DC 20008.

*Contact Person:* Katherine M. Woodbury, Phd, Scientific Review Administrator, National Institute of Neurological Disorders and Stroke, National Institutes of Health, PHS, DHHS, Federal Building, Room 9C10, 7550 Wisconsin Avenue, Bethesda, MD 20892, 301-496-9223.

*Name of Committee:* Training Grant and Career Development Review Committee.

*Date:* February 19, 1999.

*Time:* 8 AM to 5 PM.

*Agenda:* To review and evaluate grant applications.

*Place:* Washington Monarch Hotel, 2401 "M" Street NW, Washington, DC 20037.

*Contact Person:* Lillian M. Pubols, Phd, Chief, Scientific Review Branch, Scientific Review Branch, Division of Extramural Activities, NINDS, National Institutes of Health, PHS, DHHS, Federal Building, Room 9C10, 7550 Wisconsin Avenue, Bethesda, MD 20892-9175, 301-496-9223, Ip28e@nih.gov.

*Name of Committee:* National Institute of Neurological Disorders and Stroke Initial Review Group Neurological Sciences and Disorders B.

*Date:* February 25-26, 1999.

*Time:* 7:30 AM to 5 PM.

*Agenda:* To review and evaluate grant applications.

*Place:* The Hotel Washington, 15 15th Street NW, Washington, DC 20004-1099.

*Contact Person:* Paul A. Sheehy, Phd, Scientific Review Administrator, National Institute of Neurological Disorders and Stroke, National Institutes of Health, PHS, DHHS, Federal Building, Room 9C10, 7550 Wisconsin Avenue, Bethesda, MD 20892-9175, 301-496-9223.

(Catalogue of Federal Domestic Assistance Program Nos. 93.853, Clinical Research Related to Neurological Disorders; 93.854, Biological Basis Research in the Neurosciences, National Institutes of Health, HHS)

Dated: December 30, 1998.

#### **LaVerne Y. Stringfield,**

*Committee Management Officer, National Institutes of Health.*

[FR Doc. 99-237 Filed 1-5-99; 8:45 am]

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